REMARKS

The Official Action dated April 13, 2007 and the references cited therein have been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, the Examiner indicates that newly presented claims 44 and 45 have been withdrawn from consideration for allegedly encompassing non-elected subject matter. Accordingly, claims 1-9, 11-22 and 24-26 are currently being examined on the merits.

Claims 1, 2, 7-9, 11-15, 20-22 and 24-26 stand rejected under 35 U.S.C. §112, first paragraph as the specification allegedly fails to enable the full scope of the claims. These claims also stand rejected as allegedly failing to comply with the written description of the statute. Specifically, the Examiner appears to contend that the term "agent" is overly broad.

At page 7 of the Official Action, the Examiner has rejected claims 1-9, 12-22, 25 and 26 under 35 U.S.C. §102(e) as allegedly anticipated by US Patent 6,011,138 to Reff et al. Claims 1, 11, 14, and 24 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over the '138 patent to Reff et al. in view of Cockcroft et al.

Claims 1-9, 12-22, 25, and 26 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Flores-Romo et al. in view of US Patent 5,599,905 to Mosley et al.

At page 11 of the Official Action the Examiner has rejected claims 11 and 24 as allegedly unpatentable over Flores-Romo, in view of the '905 patent to Mosley and further in view of Cockcroft et al.

The Examiner has also rejected claims 1-9, 11-22 and 24-26 on the ground of non-staturory obviousness-type double patenting as being unpatentable over claims 1-24 of US Patent 6,630,140.

The foregoing objections and rejections constitute all of the grounds set forth in the April 13, 2007 Official Action for refusing the present application. Each of these objections and rejections are traversed for the reasons set forth below.

CLAIMS 1, 2, 7-9, 11-15, 20-22 AND 24-26 AS AMENDED, SATISFY THE ENABLEMENT REQUIREMENT OF 35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner has rejected claims 1, 2, 7-9, 11-15, 20-22 and 24-26 for failing to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph. Specifically, the Examiner asserts that the specification does not appear to teach "agents" other than antibodies which bind FcεRII (i.e., CD23). Applicants respectfully disagree with this contention. Indeed, at pages 18 and 19 nucleic acids encoding the FcεRII binding ligands as the "agents" encompassed by the claims are described.

Applicants vigorously dispute the Examiner's contention that the present invention is not enabling for any "agent". However, in order to expedite prosecution of the present application, the term "agent" in claim 1 has been replaced with the phrase "ligand that binds FcεRII receptor protein selected from the group consisting of an isolated protein, an isolated polypeptide, and a synthetic peptide". As noted at page 6 of the Official Action, the Examiner does acknowledge that the specification teaches ligands.

Applicants respectfully submit that specification fully enables the subject matter of claim 1. Several examples of biochemical assays utilizing FcεRII binding ligands are disclosed and include for example Western blotting, immunofluoresence and FACS analysis. The skilled person could readily adapt these assays to identify proteinaceous molecules which bind FcεRII receptor protein, disrupt binding of IgE to the same and then assess whether such agents inhibited induction of the asthmatic state as taught in Example I of the specification. The molecules exemplified provide guidance to the skilled artisan as to starting materials. As the Federal Circuit noted in In In re Wands, 8 USPQ2d 1400 (1988), engaging in experimentation to practice a claimed invention does not render the disclosure non-enabling as long as the experimentation required is not "undue". The Court stated that: "The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness . . . The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

To gain reasonable protection for the invention, the Applicants should be allowed claims that cover the ligands disclosed. Notably, variant ligands are disclosed in the application, e.g., polyclonal, monoclonal, Fab and ScFv antibodies which bind CD23. The skilled artisan can readily envisage variants of the sequences provided that would be fully functional but would have a slightly different sequence to the one disclosed in the application. Applicants should reasonably be allowed to protect such proteinaceous ligand variants. Given the explicit disclosure of a reduction to practice of the types of ligands encompassed by the claims, Applicants submit that the present claims are enabled. Accordingly, the rejection of the claims under §112, first paragraph for inadequate enablement is untenable and should be withdrawn.

CLAIMS 1, 2, 7-9, 11-15, 20-22 AND 24-26, AS AMENDED, SATISFY THE WRITTEN DESCRIPTION REQUIREMENT OF 35 U.S.C. § 112, FIRST PARAGRAPH

It is the Examiner's position that claims fail to satisfy the written description requirement under 35 U.S.C §112, first paragraph. Specifically, the Examiner asserts that the specification fails to provide an adequate written description to reasonably convey that the Applicants had possession of the methods claimed. Applicants respectfully disagree.

It is without question that the skilled artisan having the present specification before him would fully appreciate that the present inventors were in possession of inhibiting induction of an asthmatic state via administration of ligands which disrupt binding of IgE to the FcεRII receptor protein.

As mentioned above, in the interest of expediting prosecution of the instant application, Applicants have amended claims 1 and 14 to replace the term agent with the phrase "ligand that binds FcεRII selected from the group consisting of an isolated protein, an isolated polypeptide, and a synthetic peptide" Support for this amendment can be found in original claims 2 and 15.

Given the breadth of Applicants disclosure, it would be inequitable to Applicants for the USPTO to insist upon the limitation of the claims to only one type of ligand. As stated in In re Goffe, 191 USPQ 429 (CCPA 1976):

"For all practical purposes, the Board would limit Appellant to claims involving the specific materials disclosed in the examples, so that a competitor seeking to avoid infringing the claims would merely have to follow the disclosure in the subsequently issued patent to find a substitute. However, to provide effective incentives, claims must adequately protect inventors."

The claims now require that the ligand be a proteinaceous molecule that binds FcεRII which is selected from the group consisting of an isolated protein, an isolated polypeptide, and a synthetic peptide. The claims further require that the ligand disrupt binding of IgE to FcεRII in order to inhibit induction of the asthmatic state or diminish asthmatic symptoms. Applicants submit that the subject matter encompassed by the claims has been described in such a way as to convey possession of the instant method as of the filing date of the application.

The Examiner contends that Applicants have not addressed the structure of the agents previously encompassed by the claims. However, even if Applicants had not provided the protein structure of the ligands which bind FcεRII (which they have), the Examiner's attention is respectfully drawn to the recent Federal Circuit decision Falkner v. Inglis, where the Court held that "there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." Falkner v. Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006). Thus, the Examiner's requirement appears to be misplaced and contrary to recent case law.

In light of the foregoing remarks and the disclosure of several proteinaceous lignds which bind FcεRII receptor protein, it cannot be reasonably maintained that the specification does not prove a full written description of the claimed subject matter. Applicants submit that the amended claims and the specification provide sufficient identifying characteristics of the invention to meet the written description requirement under 35 U.S.C. §112, first paragraph. Accordingly, Applicant request that the rejection of the claims on this basis be withdrawn.

US PATENT 6,011,138 TO REFF ET AL. IS NOT PROPERLY CITABLE AGAINST THE CLAIMS IN THE PRESENT APPLICATION

Attached hereto is a complete copy of the Declaration under 37 C.F.R. §1.131 filed in the parent application providing evidence of conception and reduction to practice which predates the filing date of the Reff et al. patent. In light of this submission, it is clear that the '138 patent is not properly citable against the present claims. Accordingly, the rejection of claims 1-9, 12-22, 25 and 26 as lacking novelty over this patent is inappropriate and should be withdrawn.

The Examiner has also combined the '138 patent with the disclosure of Cockcroft et al. to arrive at the rejection of claims 1, 11, 14, and 24 as allegedly unpatentable under 35 U.S.C. §103(a). As above, this rejection is improper and should be withdrawn as the disclosure in the '138 patent is not properly citable against the present claims.

CLAIMS 1-9, 12-22, 25 AND 26 AS AMENDED ARE PATENTABLE OVER THE COMBINED DISCLOSURES OF FLORES-ROMO ET AL. IN VIEW OF US PATENT 5,599,905 TO MOSLEY ET AL.

The Examiner has rejected the aforementioned claims as allegedly obvious over the disclosures in Flores-Romo et al. in view of the '905 patent to Mosley. The Examiner asserts that "Flores-Romo et al. taught that administering polyclonal antibodies that bind human CD23 inhibits the synthesis of IgE both in vitro and in vivo and that regulation of IgE synthesis by CD23 is important in allergic diseases". Applicants respectfully disagree with the Examiner's characterization of the teachings in the Flores Romo et al. research article. Indeed, the abstract correctly reads that CD23 ….**could be** important in allergic diseases.

The criterion for determining obviousness under §103 is whether the prior art supplies some motivation or incentive to one of ordinary skill in the art to arrive at the invention as claimed. In re Dow Chemical Company, 5 U.S.P.Q. 2d 1929 (Fed. Cir. 1988). Moreover, all claim recitations must be considered in determining obviousness under 35 USC §103. *In re Saether*, 181 USPQ 36 CCPA 1974. Indeed, it is error to

ignore specific recitations that distinguish the claimed subject matter over the prior art. *In re Glass*, 176 USPQ 489 (CCPA 1973).

Claims 1 and 14 as amended are drawn to methods for inhibiting the induction of the asthmatic state or diminishing asthmatic symptoms via the administration of a ligand that binds FcεRII receptor protein, said ligand being selected from the group consisting of an isolated protein, an isolated polypeptide, and a synthetic peptide wherein said binding of said ligand inhibits binding of IgE to the FcεRII receptor protein, said ligand being delivered in an amount effective to alleviate asthma. Flores-Romo et al. describe inhibition of IgE synthesis in vivo in rats injected with pertussis toxin and the protein antigen ovalbumin via the administration of a rabbit antibody directed to CD23. In this artificial system, these investigators show that the production of ovalbumin specific IgE is decreased. Notably, this treatment also resulted in a significant reduction of IgG antibody levels as well. See page 1040, first column. While these researches did observe a reduction of IgE levels on B-lymphocytes, it is wholly unclear what such a reduction on CD23 levels on B cells would have on the alleviation of asthmatic symptoms as instantly claimed. Indeed, at page 1040, second column, Flores-Romo et al. disclose that at least two possibilities exist for the mechanism of action of the anti-CD23 antibody described in IgE synthesis: either Rb55 sends an intracellular signal through CD23 or blocks CD23 function during B cell-T cell interactions. Again, the relationship of these interactions with a reduction of asthmatic symptoms is wholly unclear. These researchers conclude with the following statements: "On the basis of these observations, we **speculate** that in rats immunized with pertussis and ovalbumin, T cell-associated CD23 interacts with B cell-expressed CD21, leading to an increase in IgE production in vivo. In conclusion these results demonstrate that CD23 plays a central role in the control of IgE production in vivo." This statement coupled with the speculation in the abstract which states that CD23 **could** be important in allergic diseases fails to provide the disclosure necessary to serve as a primary reference for a rejection based on a combination of reference.

The Examiner attempts to supplement the deficiencies in the Flores-Romo reference via combination with the disclosure in the '905 patent to Mosley et al. These researchers report that administration of soluble Il-4 receptor proteins blocks IgG1 and

IgE secretions and thus may be efficacious for the treatment of hypersensitivity reactions such as bronchial asthma. Notably, the agents described in Mosley et al. are completely unrelated to the ligands encompassed by Applicants claims. Moreover, neither Flores-Romo et al. nor Mosley et al. teach the administration of a ligand that binds FcεRII protein for the reduction of asthmatic symptoms. While Applicants do not dispute that soluble IL-4 receptor protein may diminish IgE levels, it is submitted that soluble IL-4 exerts a plethora of biological effects. Based on all the foregoing, it cannot be reasonably maintained that the **combined** disclosures in Flores-Romo and Mosley teach each and every element of Applicants claims nor does this combination of references place Applicants invention in the hands of the public. Indeed, the Examiner is reminded that "silence in a reference is not a proper substitute for adequate disclosure of facts from which a conclusion of obviousness may justifiably follow". In re Burt, 148 U.S.P.Q. 548 (CCPA 1966).

As a result of the recent U.S. Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, S.Ct. 2007 WL1237837 (U.S.), the U.S. Patent and Trademark Office issued a memorandum instructing examiners that, in formulating a rejection under 35 USC §103(a), based upon a combination of prior art elements, "it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed". See May 3, 2007 memo of M.A. Focarino, Deputy Commissioner for Patent Operations. In the present case, the examiner has failed to identify a plausible reason why a person of ordinary skill in the art would have combined elements of Flores-Romo et al., with Mosley et al. in the manner claimed by applicants herein.

The Court in *KSR* stated unequivocally that its prior opinion in *Graham v. John Deere Co.*, 383 US 1 (1996) continues to define the inquiry that controls the non-obviousness analysis under §103. In so stating, the Court reaffirmed the impermissibility of utilizing hindsight in assessing non-obviousness. However, it is apparent that this is precisely what the examiner has done in the present case. How else can the examiner's reliance on Flores-Romo et al. be explained, when Flores-Romo et al. is silent about the possibility of using anti-CD23 for the treatment of asthma. Indeed, Mosley et al. does not contain the slightest suggestion to use what is disclosed therein in combination with what

is disclosed in Flores-Romo et al. *Cf., In re Avery*, 186 USPQ 161 (CCPA 1975). That being the case, it cannot reasonably be maintained that the combined disclosures of Flores-Romo et al. and Mosley et al. fairly suggest doing what the applicant has done. Accordingly, the rejection of claims 1-9, 12-22, 25 and 26 under 35 USC §103(a) based on the combination of these two references is improper. *Ex parte Stauber*, 208 USPQ 945 (Bd. Apps. 1980).

CLAIMS 11 AND 24 ARE PATENTABLE OVER THE DISCLOSURE IN FLORES-ROMO ET AL. IN VIEW OF THE '905 PATENT TO MOSLEY AND FURTHER IN VIEW OF COCKCROFT ET AL.

As mentioned above, the combination of Flores-Romo et al. with the disclosure in the '905 patent to Mosley fails to render the present claims obvious. The above-noted deficiencies are not rectified by the disclosure in Cockcroft et al. While the Examiner is correct in asserting that Cockcroft et al. teach that combining known bronchodilators for the treatment of asthma is desirable, these researchers wholly fail to teach a combination of proteinaceous ligands which bind CD23 with known bronchodilators for the alleviation of asthmatic symptoms. Accordingly, the rejection of claims 11 and 24 based on this combination of references in improper and should be withdrawn.

REJECTION BASED ON THE GROUND OF NONSTATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING

In order to expedite prosecution of the present application, Applicants hereby submit a terminal disclaimer, terminally disclaiming any patent term of the instant '913 application which would extend beyond the term of US Patent 6,630,140. Accordingly, this rejection has also been rendered moot.

CONCLUSION

It is respectfully requested that the amendments presented herewith be entered in this application, since the amendments are primarily formal, rather than substantive in nature. This amendment is believed to clearly place the pending claims in condition for

allowance. In any event, the claims as presently amended are believed to eliminate certain issues and better define other issues which would be raised on appeal, should an appeal be necessary in this case.

In view of the amendments presented herewith, and the foregoing remarks, it is respectfully urged that the rejections set forth in the April 13, 2007 Official Action be withdrawn and that this application be passed to issue. In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to call the undersigned at the phone number given below.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
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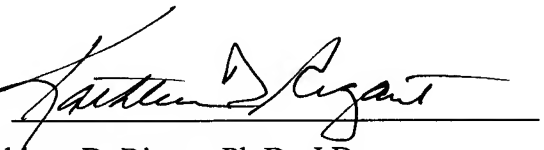
By 
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